

# Gene Therapy Trial Yields Promising Outcomes

## VITALS

**Major Finding:** Patients with NYHA stage III or IV heart failure who received gene therapy with MYDICAR had cardiovascular-related hospital stays that averaged 2 fewer days than those who received placebo.

**Data Source:** A phase II study of 39 patients enrolled in the CUPID trial.

**Disclosures:** Celladon Corp. funded the trial. Dr. Greenberg said that he had no relevant financial disclosures.

BY DOUG BRUNK

FROM THE ANNUAL MEETING  
OF THE HEART FAILURE  
SOCIETY OF AMERICA

SAN DIEGO – In a phase II study of patients with advanced heart failure, gene therapy with MYDICAR was found to be safe and was associated with benefit in clinical outcomes, symptoms, func-

tional status, and cardiac structure.

Deficiency of the protein SERCA2a is central to the progression of heart failure, resulting in abnormal calcium transfer and impairing myocardial relaxation and contraction, Dr. Barry H. Greenberg said.

MYDICAR, manufactured by Celladon Corp., is an enzyme replacement therapy that is designed to restore levels of SERCA2a. A viral

vector delivers the SERCA2a gene.

The objectives of the study, known as CUPID (Calcium Up-Regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease), were to evaluate safety and feasibility and to explore the activity and efficacy of MYDICAR in patients with advanced heart failure, said Dr. Greenberg, professor of medicine and director of the Ad-

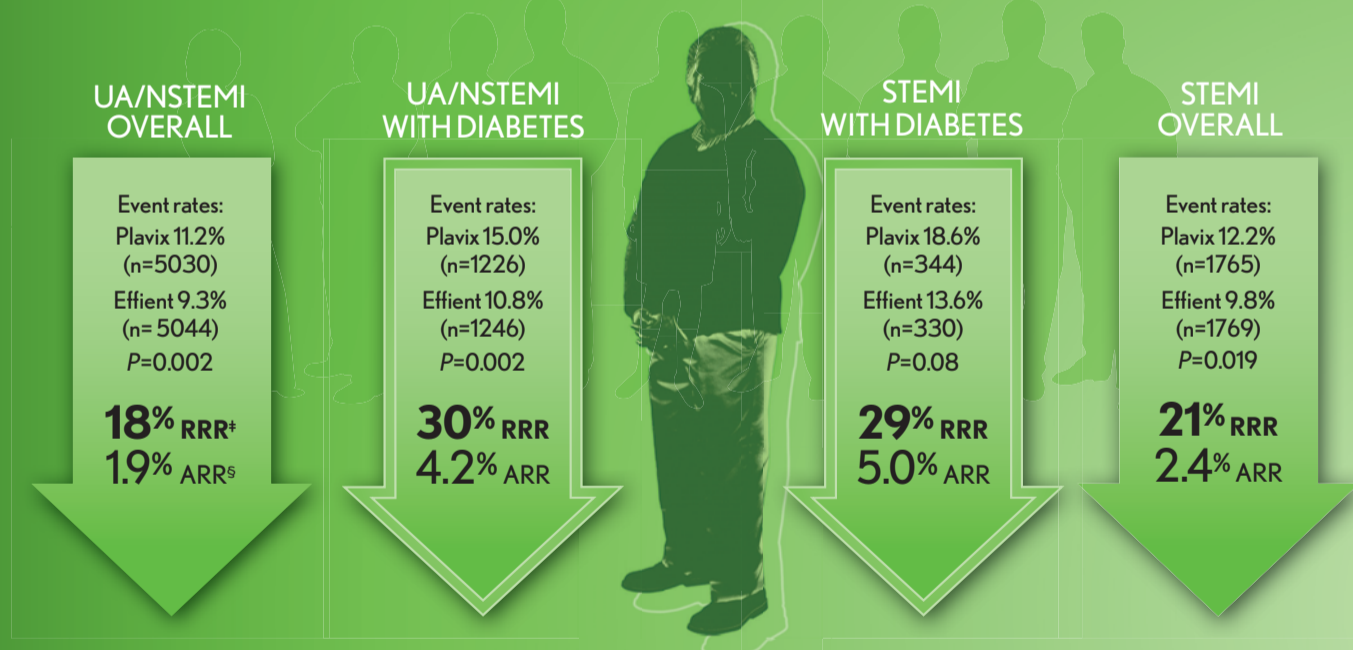
## INDICATIONS AND USAGE

Effient is indicated to reduce the rate of thrombotic CV events (including stent thrombosis) in UA/NSTEMI patients who are to be managed with PCI and in STEMI patients when managed with primary or delayed PCI



## REDUCTIONS IN THROMBOTIC CV EVENTS: TRITON-TIMI 38 DIABETES SUBGROUPS<sup>\*†,‡</sup>

The greater reduction in the primary composite endpoint in patients with diabetes treated with Effient plus ASA compared with Plavix plus ASA was consistent with those observed in the overall UA/NSTEMI and STEMI populations



\*As measured by reduction in the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke. †The loading dose of Effient was 60 mg followed by a 10-mg daily dose (plus ASA) and the loading dose of Plavix was 300 mg followed by a 75-mg daily dose (plus ASA). ‡Relative risk reduction. §Absolute risk reduction.

- In the overall study, the benefit in each population was primarily driven by a significant reduction in nonfatal MIs, with no significant differences in CV death or nonfatal stroke<sup>1</sup>
  - Approximately 40% of MIs occurred periprocedurally and were detected solely by changes in CK-MB
- In TRITON-TIMI 38, the loading dose of Plavix was delayed relative to the placebo-controlled trials that supported its approval for ACS
- TRITON-TIMI 38 was not prospectively designed or powered to determine if Effient would have greater efficacy over Plavix in the UA/NSTEMI or STEMI diabetes subgroups alone

### SELECTED SAFETY, INCLUDING SIGNIFICANT BLEEDING RISK

Effient can cause significant, sometimes fatal, bleeding. With the dosing regimens used in TRITON-TIMI 38, major and minor bleeding events were more common with Effient plus ASA compared with Plavix plus ASA.

vanced Heart Failure Treatment Program at the University of California, San Diego.

To be eligible for the trial, patients had to be 18-75 years old, have New York State Heart Association class III or IV heart failure caused by an ischemic or nonischemic etiology, have a maximal oxygen consumption of 20 mL/kg per minute or less, have a left ventricular fraction of 35% or less, and be on a stable, optimized heart failure regimen for 30 days.

Dr. Greenberg and his colleagues randomized 39 patients to one of three MYDICAL doses or to placebo, and all were

treated via single intracoronary infusion. All patients were observed for 12 months, with primary analysis after 6 months of therapy.

CUPID's primary efficacy end point was defined as evidence of success in one of four areas: group-level analysis, individual analysis, time-to-event analysis, and duration of cardiovascular-related hospitalization analysis. All



were deemed significant ( $P$  less than .2).

CUPID met the primary efficacy end point for high-dose MYDICAL treatment group vs. placebo in three of the four areas. In the group-level analysis, significant improvements were seen in the treatment group, compared with the placebo group, in 6-minute walk tests and end systolic volume, with

**DR. GREENBERG**

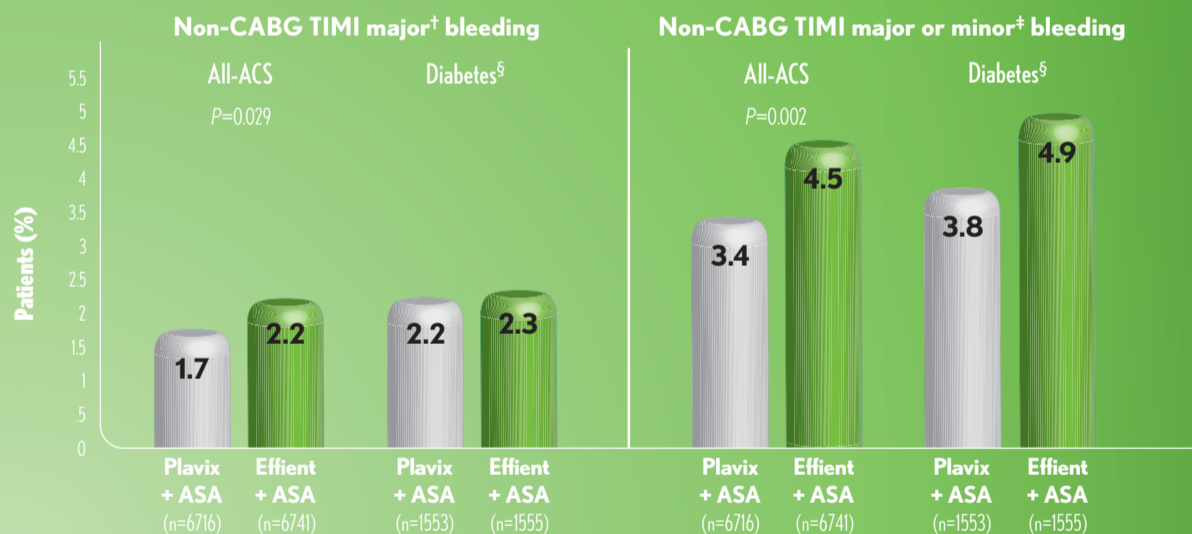
no clinically significant worsening in any end point and numerical superiority to placebo in all other end points.

In the individual analysis, the mean efficacy "score" for the treatment was significantly greater than that of the placebo group. In the time-to-death analysis, the treatment group scored numerically better than the placebo group, but the difference was not significant.

In the duration of cardiovascular-related hospitalization analysis, the duration of stay was significantly shorter for the treatment group than for the placebo group (mean, 2 fewer days). ■

**Effient**  
(prasugrel) tablets

## NON-CABG-RELATED BLEEDING: TRITON-TIMI 38 ALL-ACS POPULATION, INCLUDING DIABETES SUBGROUP<sup>\*1,4</sup>



\*Observed event rates. <sup>†</sup>Intracranial hemorrhage or clinically overt bleeding associated with a fall in hemoglobin  $\geq 5$  g/dL. <sup>‡</sup>Clinically overt bleeding associated with a fall in hemoglobin of  $\geq 3$  g/dL but  $< 5$  g/dL. <sup>§</sup> $P$  value not provided because the trial was not designed to prospectively evaluate bleeding differences in subgroups.

- In TRITON-TIMI 38, overall rates of non-CABG TIMI major and non-CABG TIMI major or minor bleeding were significantly higher on Effient than on Plavix<sup>1</sup>
- In patients who underwent CABG ( $n=437$ ), the rates of CABG-related TIMI major or minor bleeding were 14.1% with Effient plus ASA and 4.5% with Plavix plus ASA. Do not start Effient in patients likely to undergo urgent CABG<sup>1</sup>
- Patients at highest risk of bleeding were those  $\geq 75$  years of age and/or those  $< 60$  kg (132 lb)<sup>1</sup>
- Effient is contraindicated in patients with active pathological bleeding, such as from a peptic ulcer or ICH, or a history of TIA or stroke<sup>1</sup>
  - Patients who experience a TIA or stroke while on Effient generally should have therapy discontinued

Please see Important Safety Information, including Boxed Warning regarding bleeding risk, on previous page. See also Brief Summary of Prescribing Information on adjacent pages.